REMARKS

Applicants' representative wishes to thank the Examiners for the courtesy of a telephone conference to discuss the present application. Reconsideration and withdrawal of the rejections is light of the following remarks are respectfully requested.

I. Rejections under 35 U.S.C. §103

Claims 1-3, 5, 7, 9, 10, 13, and 15-18 were rejected under 35 U.S.C. §103 as allegedly obvious over Huiying *et al.* (*Virologica Sinica*, 13:3:213 (1998)) in view of Liau *et al.* (U.S. Patent No. 6,207,439).

This rejection is respectfully traversed for the following reasons.

A. The Invention

A detailed summary of the invention was provided in the response submitted October 30, 2003. A brief summary is provided here to facilitate the following remarks.

The Examiner is respectfully requested to consider the attached Declaration Under 37 C.F.R. §1.132 executed by Dr. Asato Kojima. As set forth in Point 3 of Dr. Kojima's declaration, the present invention includes an inactivated virus particle, which achieves a neutralizing antibody titer of the anti-serum obtained by immunization that is about twice to about 10 times the neutralizing antibody titer of the anti-serum obtained by immunization with inactivated virus particles prepared from virus cultured in mouse brain.

As further set forth in Point 3 of Dr. Kojima's Declaration, the inactivated virus particle of the present invention is prepared by a process comprising a step of inactivation followed by a step of purification solely by physical means. This methodology results in a virus particle having an unaltered surface (Fig. 1B) that preserves the correct steric conformation for presentation of the antigen to antibodies, leading to the high neutralizing antibody titer.

B. The Cited Art

HUIYING ET AL. relates to a method for large scale purification of Japanese encephalitis (JE) vaccine in Vero cells by (1) concentrating by ultrafiltration; (2) precipitating with protamine sulfate; and then (3) purifying by zonal centrifugation at non-continuous sucrose gradients. As discussed in Point 4 of Dr. Kojima's Declaration, Huiying *et al.* disclose that zonal centrifugation is used to purify a concentrated vaccine which has already undergone inactivation, ultrafiltration, concentration, and protamine sulfate precipitation. Therefore, a step of inactivation is followed by a chemical treatment step before the step of zonal centrifugation.

LIAU ET AL. disclose a process for large-scale purification of a live Japanese encephalitis virus from JEV-infected mouse brains and cell cultures. As discussed in Point 5 of Dr. Kojima's Declaration, Liau *et al.* disclose JEV from mouse brain or cell culture purified by microfiltration, ultrafiltration, and liquid chromatography and then inactivated. Importantly, Liau *et al.* do not distinguish between the results obtained with JEV from mouse brain or cell culture.

C. Analysis

According to the MPEP § 2143, "to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art references (or references when combined) must teach or suggest all the claim limitations."

It is insufficient that the prior art discloses the components of the claimed invention, either separately or used in other combination; there must be some teaching, suggestion or incentive to make the combination made by the inventor. (Northern Telecom Inc. v. Datapoint Corp., 15 USPQ2nd 1321 (CAFC 1990)).

As discussed above, the present invention relates to inactivated viral particles prepared by a process of (i) inactivation followed by (ii) purification solely by physical means.

Huiying *et al.* teach inactivation of a vaccine, chemical purification by protamine sulfate precipitation to remove the cell DNA, and physical purification by zonal centrifugation to remove non-viral protein.

Liau *et al.* teach physical purification of a JEV infected cell culture, which is then inactivated.

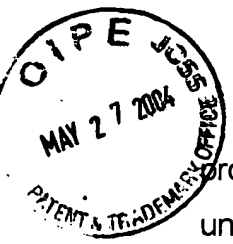
As discussed in Point 6 of Dr. Kojima's Declaration, to prepare the vaccine of the present invention, one would need to omit the physical purification step disclosed in Huiying *et al.* and still obtain a neutralizing antibody titer that is about twice to about 10 times the neutralizing antibody titer of an anti-serum obtained by immunization with inactivated virus particles prepared from virus cultured in mouse brain.

Those of skill in the art believed at the time that the step of chemical purification was necessary to remove the Vero cell DNA and would not be motivated to omit this step. Liau *et al.*, although omitting the chemical treatment step, show a different order of steps. Liau *et al.* further are silent regarding any difference in the neutralizing antibody titer of virus particles prepared from cell culture in comparison to virus particles prepared from mouse brain. Thus, one of skill in the art has no way of knowing if one would achieve the high neutralizing antibody titer found with the precise order and steps of the present invention. Therefore, there is no motivation to omit the chemical treatment step of protamine sulfate precipitation.

Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §103.

Conclusion

In view of the foregoing, Applicants submit that the claims pending in the application are in condition for allowance. A Notice of Allowance is therefore respectfully requested.



If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4410.

Respectfully submitted,

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Date: May 27, 2004

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